

Applicants : NALDINI, et al.
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In The Claims:

Please amend claims as follows:

1. (Original) A bidirectional promoter for expression of at least two coding sequences in opposite direction in animal cells comprising 5' end to 3' end:

a) a first minimal promoter sequence derived from cytomegalovirus (CMV) or mouse mammary tumor virus (MMTV) genomes;

b) a full efficient promoter sequence derived from an animal gene;

the two promoter sequences driving a coordinate transcription of said coding sequences in the opposite orientation.

2. (Original) The bidirectional promoter according to claim 1 wherein the full efficient promoter sequence consists of an enhancer region and a second minimal promoter sequence.

3. (Original) The bidirectional promoter according to claim 1 wherein the full efficient promoter sequence derives from ubiquitously expressed genes comprising the phosphoglycerate kinase or the ubiquitin gene.

4. (Currently Amended) A bidirectional expression cassette essentially comprising the bidirectional promoter according to ~~previous~~ claims 1, convenient insertion sites positioned downstream to each promoter, and polyadenylation sites positioned downstream to each insertion site.

5. (Original) The bidirectional expression cassette according to claim 4 further comprising at least one post-transcriptional

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regulatory element positioned upstream to one or each polyadenylation site.

6. (Currently Amended) The bidirectional expression cassette according to claim 4 ~~or 5~~ further comprising at least one internal ribosome entry site (IRES) sequence to express three or more genes.

7. (Currently Amended) An expression construct containing the bidirectional promoter according to claim 1 ~~or 2~~.

8. (Currently Amended) An expression construct containing the bidirectional expression cassette according to claims 4-6.

9. (Currently Amended) A gene transfer expression vector containing the expression construct according to claims 7 ~~or 8~~ further comprising lentiviral or retroviral sequences.

10. (Currently Amended) ~~Use of~~ A Method for the delivery and expression of multiple genes in animal cells comprising the gene transfer expression vector according to claim 9 ~~for the delivery and expression of multiple genes in animal cells.~~

11. (Currently Amended) ~~Use of the gene transfer expression vector~~ The Method according to claim 10 wherein animal cells are tissue animal cells ~~in~~ ex vivo.

12. (Currently Amended) ~~Use of the gene transfer expression vector~~ The Method according to claim 11 wherein tissue animal cells are comprising brain neurons.

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13. (Currently Amended) A Method for the coordinate expression of two exogeneous coding sequences into an animal cell comprising the following steps:

- a) cloning said coding sequences into the gene transfer expression vector according to claim 9, each coding sequence under the control of one of the two promoters of the bidirectional promoter;
- b) transforming animal cells by means of said vectors; and
- c) allowing the expression of the vector.

14. (Currently Amended) The Method for the coordinate expression of two exogeneous coding sequences according to claim 10 wherein the animal cell is an human cell.

15. (Currently Amended) The Method for the coordinate expression of two exogeneous coding sequences according to claim 14 wherein the human cell is a retransplantable human cell.

16. (Currently Amended) The Method for the coordinate expression of two exogeneous coding sequences according to claim 15 wherein the retransplantable human cell is an hematopoietic cell.

17. (Currently Amended) A Method for generating a transgenic non human organism comprising the step of transforming appropriate cells with an expression construct containing the bidirectional cassette according to claims 7 ~~or~~ 8.

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18. (Currently Amended) A Method for generating a transgenic non human organism comprising the step of transforming appropriate cells by means of the gene transfer expression vector according to claim 9.

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On a new page after the claims, please add the below paragraph starting on line 1:

**LENTIVIRAL VECTORS CARRYING SYNTHETIC BI-DIRECTIONAL
PROMOTERS AND USES THEREOF**

ABSTRACT OF THE INVENTION

-- It is described a bidirectional promoter for expression of at least two coding sequences in opposite direction in animal cells; bidirectional expression cassettes; expression constructs; gene transfer expression vectors; and methods for the use thereof.--